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NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 9 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enhanced
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NEWS 12 MAR 22 PATDPASPC - New patent database available
NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 14 APR 04 EPFULL enhanced with additional patent information and new fields
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FULL ESTIMATED COST
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FILE LAST UPDATED: 26 Apr 2005 (20050426/ED)

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=> hcv/bi,ab
HCV IS NOT A RECOGNIZED COMMAND
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=> s hcv/bi,ab 9043 HCV/BI 8595 HCV/AB
L1 9043 HCV/BI,AB

=> s (hepatitis(w)c)/bi,ab 47012 HEPATTITIS/BI
37966 HEPATTITIS/AB 3296295 C/BI
3126291 C/AB
L2 13330 (HEPATTITIS(W)C)/BI,AB

=> s l1 or l2
L3 13947 L1 OR L2

=> s odn3/bi,ab 10 ODN3/BI 8 ODN3/AB
L4 10 ODN3/BI,AB

=> s oligonucleotide#/bi,ab 75023 OLIGONUCLEOTIDE#/BI
57855 OLIGONUCLEOTIDE#/AB
L5 75023 OLIGONUCLEOTIDE#/BI,AB

=> s oligodeoxynucleotide#/bi,ab 7363
OLIGODEOXYNUCLEOTIDE#/BI 6256
OLIGODEOXYNUCLEOTIDE#/AB
L6 7363 OLIGODEOXYNUCLEOTIDE#/BI,AB

=> s oligodeoxyribonucleotide#/bi,ab 9483
OLIGODEOXYRIBONUCLEOTIDE#/BI 3493
OLIGODEOXYRIBONUCLEOTIDE#/AB
L7 9483 OLIGODEOXYRIBONUCLEOTIDE#/BI,AB

=> s l4 or l5 or l6 or l7
L8 82587 L4 OR L5 OR L6 OR L7

=> s l3 and l8
L9 596 L3 AND L8

=> s antisense/bi,ab 38114 ANTISENSE/BI 26530
ANTISENSE/AB
L10 38114 ANTISENSE/BI,AB

=> s (anti(w)sense)/bi,ab 366044 ANTI/BI 288753
ANTI/AB 35564 SENSE/BI 34004
SENSE/AB
L11 1297 (ANTI(W)SENSE)/BI,AB

=> s l10 or l11
L12 38918 L10 OR L11

=> s l8 and l12
L13 19463 L8 AND L12

=> s l9 and l12
L14 166 L9 AND L12

=> s l14 not 2005/py 341973 2005/PY
L15 136 L14 NOT 2005/PY

=> s l15 not 2004/py 1195310 2004/PY
L16 99 L15 NOT 2004/PY

=> s l16 not 2003/py 1230298 2003/PY
L17 82 L16 NOT 2003/PY

=> s l17 not 2002/py 1161634 2002/PY
L18 66 L17 NOT 2002/PY

=> s l18 not 2001/py 1103342 2001/PY
L19 49 L18 NOT 2001/PY

=> s l19 not 2000/py 1030820 2000/PY
L20 38 L19 NOT 2000/PY

=> s l20 not 1999/py 934329 1999/PY
L21 27 L20 NOT 1999/PY

=> s l21 not 1998/py 906901 1998/PY
L22 18 L21 NOT 1998/PY

=> d his
(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005

L1 9043 S HCV/BI,AB
L2 13330 S (HEPATITIS(W)C)/BI,AB
L3 13947 S L1 OR L2
L4 10 S ODN3/BI,AB
L5 75023 S OLIGONUCLEOTIDE#/BI,AB
L6 7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7 9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB
L8 82587 S L4 OR L5 OR L6 OR L7
L9 596 S L3 AND L8
L10 38114 S ANTISENSE/BI,AB

L11 1297 S (ANTI(W)SENSE)/BI,AB
L12 38918 S L10 OR L11
L13 19463 S L8 AND L12
L14 166 S L9 AND L12
L15 136 S L14 NOT 2005/PY
L16 99 S L15 NOT 2004/PY
L17 82 S L16 NOT 2003/PY
L18 66 S L17 NOT 2002/PY
L19 49 S L18 NOT 2001/PY
L20 38 S L19 NOT 2000/PY
L21 27 S L20 NOT 1999/PY
L22 18 S L21 NOT 1998/PY

=> d l22 1-18 bib ab

L22 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:415321 CAPLUS
DN 129:240824
TI Inhibition of ***hepatitis*** ***C*** virus by
antisense ***oligodeoxynucleotide*** in vitro
AU Liu, Yong; Chen, Zhi; He, Nanxiang; Liu, Kezhou; Zhang,
Mingtai; Wang, Xinzi
CS Institute of Infectious Disease, Zhejiang Medical University,
Hangzhou, 310003, Peop. Rep. China
SO Zhonghua Yixue Zazhi (1997), 77(8), 567-570 CODEN:
CHHTAT; ISSN: 0376-2491
PB Zhonghua Yixue Zazhi
DT Journal
LA Chinese
AB The inhibitory effect of ***antisense***
oligodeoxynucleotide on ***hepatitis*** ***C***
virus (***HCV***) in vitro was studied. The H9 cells
transfected by pCD- ***HCV***, a recombinant ***HCV***
contg. total ***HCV*** structural gene, were treated with 2
15-mers phosphorothioate (PS) ODNs (***oligodeoxynucleotides***) complementary (PS-ASON) and
homologous to ***HCV*** core genomic region, which were
labeled with digoxin (DIG). Spot blot hybridization was carried
out. And, rPS-ODN (a 15-mers PS ODN of random sequence) or
PS-ASON, treated by the 2 ODNs, were modified with 2
liposomes (DOTAP and lipofectin) and calcium phosphate pptn.
resp. The variation of level of ***HCV*** mRNA and
HCV antigen expression was obsd. by RT-PCR and dot
ELISA with a half-rat. PS-ODN and PS-ASON were detected in
the H9 cells. The target gene hybridized to PS-ASON and PS-
ODN labeled with DIG. Only the ***antisense*** PS-ASON
decreased ***HCV*** mRNA and ***HCV*** antigen
expression levels. PS-ODN and rPS-ODN, however, were not
effective. The time-dependent and dose-dependent inhibition of
PS-ASON was obsd. Both of liposomal PS-ASON showed more
highly effective inhibition, in contrast to free PS-ASON, but
calcium phosphate pptn.-PS-ASON complex did not. PS-ASON
did not influence the H9 cells growth at 10 .mu.mol L-1. PS-
ASON complementary to ***HCV*** core gene is asODN and
exerts ***antisense*** -inhibitory effect on the level of
HCV translation obviously, but not on the level of
HCV replication and transcription.

L22 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:758344 CAPLUS
DN 128:84071
TI Backbone modified ***antisense***
oligodeoxynucleotides directed against the
hepatitis - ***C*** -virus (***HCV***)-RNA
AU Eisenhardt, S.; Samstag, W.; Jahn-Hofman, K.; Engels, J.
W.; Renz, R.; Hofschneider, P. H.; Caselmann, W. H.; Alt, M.

CS Institute for Organic Chemistry, Johann Wolfgang-University of Frankfurt, Germany
SO Nucleosides & Nucleotides (1997), 16(7-9), 1669-1672
CODEN: NUNUD5; ISSN: 0732-8311
PB Marcel Dekker, Inc.
DT Journal
LA English
AB We synthesized 23-mer ***oligodeoxynucleotides*** (ODN's) with different modifications, directed against nt 326-348 of ***HCV*** -RNA. The ODN contains 6 modified nucleotides. The types of modification we tested are nonionic (methylphosphonates, benzylphosphonates) and ionic phosphothioates.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:295885 CAPLUS
DN 127:28649
TI Core specific ***antisense*** phosphorothioate ***oligodeoxynucleotides*** as potent and specific inhibitors of ***hepatitis*** ***C*** viral translation
AU Alt, M.; Renz, R.; Hofschneider, P. H.; Caselmann, W. H.
CS Department of Virus Research, Max-Planck-Institut fur Biochemie, Martinsried, Germany
SO Archives of Virology (1997), 142(3), 589-599 CODEN: ARVIDF; ISSN: 0304-8608
PB Springer
DT Journal
LA English
AB ***Antisense*** phosphorothioate ***oligodeoxynucleotides*** (S-ODN) complementary to sequence stretches in the 5' non-coding region (NCR) of the ***hepatitis*** ***C*** virus (***HCV***) have recently been shown to effectively inhibit viral gene expression. In order to further delineate the optimum target region in the highly conserved 5' end of the viral RNA, S-ODN 5, complementary to ***HCV*** core coding sequences were analyzed in the present study. In a rabbit reticulocyte lysate (RRL) in vitro translation assay S-ODN 5, complementary to the ***HCV*** -RNA nucleotides 340-353, and S-ODN-6, complementary to nucleotides 348-365, resulted in an inhibition of viral translation of 90.4 +/- 1.3% and 93.7 +/- 5.1%, resp. at a concn. of 4.14 .mu.M. S-ODN 7, complementary to nucleotides 371-388, was relatively inefficient and showed a maximal inhibition of 42.4 +/- 12.2%. It has been suggested that in living cells an inhibition by S-ODN is mainly mediated by the action of RNase H. In RRL the RNase H content is very low; therefore, to simulate the situation in living cells inhibition expts. in RRL enriched with RNase H were performed. Under these conditions S-ODN 5, 6 and 7 inhibited viral translation by 45.6 +/- 6.3%, 80.3 +/- 2.8% and 70.9 +/- 5.7% at concns. as low as 0.2 .mu.M. At this concn. no inhibition was obsd. in the std. RRL assay. In cell culture S-ODN 7 was by far the most efficient inhibitor of viral translation, resulting in a specific inhibition of 89.4 +/- 3.6% at a concn. of 0.3 .mu.M. Taken together with the results of our previous study, nucleotides 326-348 comprising the 3' end of the NCR and nucleotides 371-388, located entirely in the core coding region of the ***HCV*** RNA, are effective targets for S-ODN mediated inhibition of viral translation.
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:35883 CAPLUS
DN 126:153311
TI Combinatorial screening and rational optimization for hybridization to folded ***hepatitis*** ***C*** virus RNA of ***oligonucleotides*** with biological ***antisense*** activity
AU Lima, Walt F.; Brown-Driver, Vickie; Fox, Maureen; Hanecak, Ronnie; Bruce, Thomas W.
CS Dep. Res. Med. Chem., Isis Pharmaceuticals, Carlsbad, CA, 92008, USA
SO Journal of Biological Chemistry (1997), 272(1), 626-638
CODEN: JBCHA3; ISSN: 0021-9258
PB American Society for Biochemistry and Molecular Biology
DT Journal
LA English
AB We describe our initial application of a biochem. strategy, comprising combinatorial screening and rational optimization, which directly identifies ***oligonucleotides*** with max. affinity (per unit length), specificity, and rates of hybridization to structurally preferred sites on folded RNA, to the problem of design of ***antisense*** ***oligonucleotides*** active against the ***hepatitis*** ***C*** virus (***HCV***). A fully randomized sequence DNA ***oligonucleotide*** (10-mer) library was equilibrated with each of two folded RNA fragments (200 and 370 nucleotides (nt)), together spanning the 5' 440 nt of an ***HCV*** transcript (by overlapping 130 nt), which were varied over a range of concns. The equilibrations were performed in soln. under conditions detd. to preserve RNA structure and to limit all RNA-DNA library ***oligonucleotide*** interactions to 1:1 stoichiometry. Subsequent Escherichia coli RNase H (endoribonuclease H: EC 3.1.26.4) cleavage anal. identified two preferred sites of highest affinity heteroduplex hybridization. The lengths and sequences of different substitute chem. ***oligonucleotides*** complementary to these sites were rationally optimized using an iterative and quant. anal. of binding affinity and specificity. Thus, DNA ***oligonucleotides*** that hybridized with the same affinity to the preferred sites in the folded RNA fragments found by screening as to short (.ltoreq.25 nt) RNA complements were identified but were found to vary in length (10-18 nt) from site to site. Phosphorothioate (P=S) and 2'-fluoro (2'-F) uniformly substituted ***oligonucleotides*** also were found, which hybridized optimally to these sites, supporting the design of short (10-15-nt) and maximally specific ***oligonucleotides*** that are more nuclease-resistant (via P=S) and have higher affinity (via 2'-F) than DNA. Finally, the affinities of DNA and uniform 2'-F-, P=S-substituted 10-20-mer ***oligonucleotide*** complements for the best hybridization site, from ***HCV*** nt 355 to nt 364-374, closely corresponded to ***antisense*** mechanism inhibition activities in an in vitro translation assay and in a human cell-based ***HCV*** core protein expression assay, resp. These results validate our strategy for the selection of hybridization-optimized and biol. active ***antisense*** ***oligonucleotides*** targeting ***HCV*** RNA and support the potential for utility in further applications.
RE.CNT 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:609713 CAPLUS
DN 125:240209
TI PCR-based methods for detecting positive or negative strand of RNA virus
IN Yamaguchi, Kenjiro; Matsunaga, Yuka; Fukutani, Toyoji
PA Tonen Corp, Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp. CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE				
PI	JP 08187097	A2	19960723	JP 1994-338535	
	19941228				
PRAI	JP 1994-338535		19941228		

AB A method for detecting the pos. or neg. strand of a RNA virus comprises enzymic synthesizing the cDNA using ***antisense*** or sense primers. The method can be applied in the detection of the pos. and neg. strand RNA of ***hepatitis*** virus (***HCV***). Both sense and ***antisense*** primer for detecting ***HCV*** RNA are provided. The method can be used for monitoring the interferon (IFN) treatment for ***HCV*** infection.

L22 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:607254 CAPLUS

DN 125:240208

TI ***Hepatitis*** virus genotype determination by PCR-based methods

IN Yamaguchi, Kenjiro; Hasegawa, Akira

PA Tonen Corp, Japan

SO Jpn. Kokai Tokkyo Koho, 13 pp. CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE				
PI	JP 08187096	A2	19960723	JP 1994-309865	
	19941118				
PRAI	JP 1994-309865		19941118		

AB A PCR-based method for the detn. of ***hepatitis*** virus (***HCV***) genotypes by targeting the conserved 5' UTR region is described. The method comprises (1) amplification of its 5' UTR region encompassing residues 117.apprx.120 and (2) digestion of the PCR products with HaeIII. Two sets of ***oligonucleotide*** primers are provided for PCR. The method is more sensitive the prior arts (e.g. the Okamoto method). The method can be used for monitoring the treatment using interferon (IFN).

L22 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:604352 CAPLUS

DN 125:292323

TI In vitro inhibition of ***hepatitis*** virus gene expression by chemically modified ***antisense*** oligodeoxynucleotides

AU Vidalin, O.; Major, M. E.; Rayner, B.; Imbach, J.-L.; Trepo, C.; Inchauspe, G.

CS Institut National de la Sante, la Recherche Medicale U271, Lyon, 69424, Fr.

SO Antimicrobial Agents and Chemotherapy (1996), 40(10), 2337-2344 CODEN: AMACQ; ISSN: 0066-4804

PB American Society for Microbiology

DT Journal

LA English

AB The authors have explored different domains within the ***hepatitis*** virus (***HCV***) 5' noncoding region as potential targets for inhibition of ***HCV*** translation by ***antisense*** oligodeoxynucleotides*** (ODNs). Inhibition assays were performed with two different cell-free systems, rabbit reticulocyte lysate and wheat germ ext., and three types of chem. structures for the ODNs were

evaluated: natural phosphodiester (beta.-PO), .alpha.-anomer phosphodiester (.alpha.-PO), and phosphorothioates (PS). A total of six original ODNs, displaying sequence-specific inhibition ranging from 62 to 96%, that mapped in the pyrimidine-rich tract (nucleotides [nt] 104 to 127) and in the initiator AUG codon (nt 338 to 357) were identified. Two ODNs, which were targeted at the initiator AUG (nt 341 to 367 and 351 to 377) and which had been previously described as active against genotype 1b and 2a sequences, were shown to exhibit inhibition of expression (>95%) of a type 1a sequence. Control expts. with the irrelevant chloramphenicol acetyltransferase sequence as a marker and randomized ODNs demonstrated that levels of inhibition assocd. with the use of PS compds. (or as much as 94%) were mainly due to nonspecific effects. Both .alpha.- and .beta.-PO ODNs were found equally active, and no difference could be seen in the activity of .beta.-PO when it was tested in either rabbit reticulocyte lysate or wheat germ ext., suggesting that RNase H-independent mechanisms may be involved in the inhibitions obsd. However, specific RNA cleavage products generated from .beta.-PO inhibition expts. could be identified, indicating that, with these compds., control of translation also involves RNase H-dependent mechanisms. This study further delimits the existence of favorable target sequences for the action of ODNs within the ***HCV*** 5' noncoding region and indicates the possibility of using nuclease-resistant .alpha.-PO compds. in cellular studies.

L22 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:484299 CAPLUS

DN 125:213586

TI Characterization of cell lines allowing tightly regulated expression of ***hepatitis*** virus core protein
AU Moradpour, Darius; Englert, Christoph; Wakita, Takaji; Wands, Jack R.

CS Molecular Hepatology Lab., Harvard Medical Sch., Charlestown, MA, 02129, USA

SO Virology (1996), 222(1), 51-63 CODEN: VIRLAX; ISSN: 0042-6822

PB Academic

DT Journal

LA English

AB A tetracycline-regulated system was used to generate cell lines allowing tightly controlled expression of a ***hepatitis*** virus (***HCV***) cDNA comprising the 5' noncoding, the core, and part of the E1 regions. Prodn. of 21-kDa processed nucleocapsid protein could be regulated over a broad range by the concn. of tetracycline present in the culture medium. Induction ratios of over 1000-fold were found using an ***HCV*** core-luciferase fusion construct. Core protein had an intracellular half-life of 9 h and corresponded to the product of 173 amino-terminal amino acids of the ***HCV*** open reading frame. Sequential immunofluorescence microscopy revealed the presence of core antigen first in a predominantly perinuclear fine-reticular staining pattern and subsequently also in cytoplasmic granules and vesicles. By immunoelectron microscopy core protein was found on the endoplasmic reticulum membrane and on the surface of cytoplasmic lipid droplets. Growth rate analyses and colony formation efficiency assays showed no major cytotoxic effect of ***HCV*** core protein expression per se. ***HCV*** gene expression could be inhibited by an ***antisense*** oligonucleotide*** targeting a region immediately downstream of the translation initiation codon. These cell lines represent important tools to investigate structural and functional properties of ***HCV*** core protein and may be useful to evaluate gene therapeutic strategies against ***HCV*** in a cellular system.

L22 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:433085 CAPLUS
DN 125:159621
TI ***Antisense*** ***oligonucleotide*** inhibition of
hepatitis ***C*** virus gene expression in
transformed hepatocytes
AU Hanecak, Ronnie; Brown-Driver, Vickie; Fox, Maureen C.;
Azad, Raana F.; Furusako, Shoji; Nozaki, Chikateru; Ford,
Clifford; Sasmor, Henri; Anderson, Kevin P.
CS Department Infectious Diseases, Isis Pharmaceuticals,
Carlsbad, CA, 92008, USA
SO Journal of Virology (1996), 70(8), 5203-5212 CODEN:
JOVIAM; ISSN: 0022-538X
PB American Society for Microbiology
DT Journal
LA English
AB Genetic and biochem. studies have provided convincing
evidence that the 5' noncoding region (5' NCR) of
hepatitis ***C*** virus (***HCV***) is highly
conserved among viral isolates worldwide and that translation of
HCV is directed by an internal ribosome entry site (IRES)
located within the 5' NCR. We have investigated inhibition of
HCV gene expression using ***antisense***
oligonucleotides complementary to the 5' NCR,
translation initiation codon, and core protein coding sequences.
Oligonucleotides were evaluated for activity after
treatment of a human hepatocyte cell line expressing the
HCV 5' NCR, core protein coding sequences, and the
majority of the envelope gene (E1). More than 50
oligonucleotides were evaluated for inhibition of
HCV RNA and protein expression. Two
oligonucleotides, ISIS 6095, targeted to a stem-loop
structure within the 5' NCR known to be important for IRES
function, and ISIS 6547, targeted to sequences spanning the
AUG used for initiation of ***HCV*** polyprotein translation,
were found to be the most effective at inhibiting ***HCV***
gene expression. ISIS 6095 and 6547 caused concn.-dependent
redns. in ***HCV*** RNA and protein levels, with 50%
inhibitory concns. of 0.1 to 0.2 .mu.M. Redn. of RNA levels, and
subsequently protein levels, by these phosphorothioate
oligonucleotides was consistent with RNase H cleavage
of RNA at the site of ***oligonucleotide*** hybridization.
Chem. modified ***HCV*** ***antisense***
phosphodiester ***oligonucleotides*** were designed and
evaluated for inhibition of core protein expression to identify
oligonucleotides and ***HCV*** target sequences
that do not require RNase H activity to inhibit expression. A
uniformly modified 2'-methoxyethoxy phosphodiester
antisense ***oligonucleotide*** complementary to
the initiator AUG reduced ***HCV*** core protein levels as
effectively as phosphorothioate ***oligonucleotide*** ISIS
6095 but without reducing ***HCV*** RNA levels. Results of
our studies show that ***HCV*** gene expression is reduced
by ***antisense*** ***oligonucleotides*** and
demonstrate that it is feasible to design ***antisense***
oligonucleotide inhibitors of translation that do not
require RNase H activation. The data demonstrate that chem.
modified ***antisense*** ***oligonucleotides*** can be
used as tools to identify important regulatory sequences and/or
structures important for efficient translation of ***HCV***.

L22 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1996:133731 CAPLUS
DN 124:193313
TI Phosphorothioate ***antisense***
oligodeoxynucleotides capable of inhibiting

hepatitis ***C*** virus gene expression: in vitro
translation assay
AU Seki, Makoto; Honda, Yoshikazu
CS Biosciences Laboratory, Mitsubishi Chemical Corporation,
Yokohama, 227, Japan
SO Journal of Biochemistry (Tokyo) (1995), 118(6), 1199-204
CODEN: JOBIAO; ISSN: 0021-924X
PB Japanese Biochemical Society
DT Journal
LA English
AB Phosphorothioate ***antisense***
oligodeoxynucleotides (S-ODNs) designed to hybridize to
the 5' region of the ***hepatitis*** ***C*** virus (
HCV) genome were evaluated as to their ability to inhibit
HCV gene expression, using an in vitro translation
system. Three effective regions were found to interfere with the
translation of ***HCV*** RNAs. These regions were region A
[nucleotides (nt) 124 to 153], region B (nt 100 to 123), and
region C (nt 324 to 360). Further detailed evaluation of S-ODNs
within each region allowed us to propose some ***HCV*** -
specific antiviral agent candidates. Two of them, SMS16 (nt 328
to 347) and SMS17 (nt 326 to 345), caused over 90% inhibition
of ***HCV*** gene expression when present in a less than
fourfold molar excess; this effect was sequence-specific and
dose-dependent.

L22 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1995:872871 CAPLUS
DN 124:75623
TI Specific inhibition of ***hepatitis*** ***C*** viral
gene expression by ***antisense*** phosphorothioate
oligodeoxynucleotides
AU Alt, Michael; Renz, Renate; Hofschneider, Peter H.;
Paumgartner, Gustav; Caselmann, Wolfgang H.
CS Department Virus Research, Max-Planck-Institut fur
Biochemie, Martinsried, 0-82152, Germany
SO Hepatology (Philadelphia) (1995), 22(3), 707-17 CODEN:
HPTLD9; ISSN: 0270-9139
PB Saunders
DT Journal
LA English
AB The inhibitory effect of ***antisense***
phosphorothioate ***oligodeoxynucleotides*** (S-ODN) on
hepatitis ***C*** viral gene expression was analyzed
in an in vitro test system and in cell culture. S-ODN were
directed against different stem loop structures in the 5'noncoding
region (NCR) of the ***hepatitis*** ***C*** virus (
HCV) RNA and against a nucleotide stretch, including the
start codon of the polyprotein precursor. The inhibitory effect of
these S-ODN was quantified employing a viral RNA consisting of
the first 407 nucleotides of a ***HCV*** type 1b genome
fused to the coding sequence of the firefly luciferase gene. For
in vitro assays, this RNA was generated by in vitro transcription
and used as a template in a rabbit reticulocyte lysate in vitro
translation system. The prodn. of active luciferase in the
absence or presence of S-ODN was monitored using an enzymic
assay. The best results were obtained with S-ODN 4 directed
against nucleotides 326 to 348, comprising the start AUG of the
polyprotein coding sequence. With this ***oligonucleotide***
, a specific and dose-dependent effect was obsd. with a maximal
inhibition of 96% at a S-ODN concn. of 4.14 .mu.mol/L. For cell
culture expts., the hepatoblastoma cell line HepG2 was
transfected with a plasmid expressing the ***HCV*** -
luciferase fusion RNA. In this assay system S-ODN 2,
complementary to nucleotides 264 to 282 of the ***HCV***
RNA, and S-ODN 4 were most efficient and reduced the viral

translation by 96% and 94%, resp., at a concn. of 0.3 .mu.mol/L. The inhibition was specific (1) because the expression of the ***HCV*** -luciferase fusion RNA was not significantly impaired by the control S-ODN and (2) because the expression of an unrelated mRNA was not or only slightly downregulated. These data suggest that ***HCV*** gene expression can be inhibited effectively by ***antisense*** S-ODN. Therefore, this approach represents a promising perspective for the treatment of ***hepatitis*** ***C***.

L22 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN AN 1995:718559 CAPLUS DN 123:160158

TI Inhibition of ***hepatitis*** ***C*** virus replication by ***antisense*** ***oligonucleotide*** in culture cells
AU Mizutani, Tetsuya; Kato, Nobuyuki; Hirota, Masami; Sugiyama, Kazuo; Murakami, Akira; Shimotohno, Kunitada
CS Virol. Div., Natl. Cancer Cent. Res. Inst., Tokyo, 104, Japan
SO Biochemical and Biophysical Research Communications (1995), 212(3), 906-11 CODEN: BBRC9; ISSN: 0006-291X
PB Academic
DT Journal
LA English
AB ***Oligonucleotides*** complementary to the sequences contg. the initiator codon, AUG, of the core region of pos.-stranded ***hepatitis*** ***C*** virus (***HCV***) were tested for their effects on viral translation in a cell-free protein synthesis system and on viral replication. Treatment of ***HCV*** -infected MT-2C cells with the ***antisense*** ***oligonucleotide*** (10 .mu.M) had a dramatic inhibitory effect on viral replication. This result suggests that the ***antisense*** ***oligonucleotide*** complementary to the sequence close to the initiation codon of the core region might be useful as an antiviral agent against ***HCV*** replication.

L22 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN AN 1995:450837 CAPLUS DN 122:206941

TI Pestivirus translation initiation occurs by internal ribosome entry
AU Poole, Toni L.; Wang, Changyu; Popp, R. A.; Potgieter, L. N. D.; Siddiqui, Aleem; Collett, Marc S.
CS Oak Ridge Natl. Lab., Biol. Div., Oak Ridge, TN, 37831, USA
SO Virology (1995), 206(1), 750-4 CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB The role of the 385 nucleotide 5' noncoding region (NCR) in the translation of the pestivirus genome was investigated. In vitro translation of an RNA transcript contg. the 5' NCR of the bovine viral diarrhea virus (BVDV) genome followed by the coding sequence of the first gene product (p20) of the BVDV large open reading frame resulted in the synthesis of a 20-kDa polypeptide. Results from hybrid-arrest translation studies identified a region involving a predicted RNA stem-loop structure spanning nucleotides 154-216 within the 5' NCR that was important for p20 synthesis. An addnl. inhibitory ***oligonucleotide*** was complementary to the sequence at the base of this stem-loop and encompassed the initiating AUG at nucleotide 386. ***Antisense*** ***oligonucleotides*** both upstream and downstream of those that were inhibitory had no effect on p20 translation. RNA from a dicistronic expression vector in which the BVDV 5' NCR was inserted between two reporter genes. CAT and LUC, showed strong expression of the second (LUC) cistron upon

in vitro translation. This expression was dramatically reduced in an analogous construct in which nucleotides 173-236 of the 5' NCR were deleted. Similar results were obtained when RNA from these same vectors was evaluated for expression after transfection into BHK cells. These results suggest that the BVDV 5' NCR contains an internal ribosome entry site for translation initiation. This translational mechanism is similar to that shown for ***hepatitis*** ***C*** virus, further demonstrating the close relationship between viruses of these two genera within the family Flaviviridae.

L22 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN AN 1995:348419 CAPLUS DN 122:122351

TI Treatment and prevention of chronic viral hepatitis
AU Dusheiko, G. M.
CS Royal Free Hospital and School of Medicine, London, NW2 2Q3, UK
SO Pharmacology & Therapeutics (1995), 65(1), 47-73 CODEN: PHTHDT; ISSN: 0163-7258
PB Elsevier
DT Journal; General Review
LA English
AB A review with 150 refs. Chronic viral hepatitis B, C or D may lead to cirrhosis, hepatocellular failure and hepatocellular carcinoma. The morbidity of these diseases has necessitated a prolonged search for effective therapy. Interferon-.alpha. has been studied widely and remains the mainstay of treatment. Therapy for hepatitis B has now become possible with the demonstration that .alpha.-interferons inhibit hepatitis B virus (HBV) replication and that prolonged therapy can lead to a remission. A no. of other cytokines, including thymosin, are being evaluated. Currently used nucleoside analogs and anti-retroviral therapies used in human immunodeficiency virus infection have not proven useful in chronic hepatitis B. There are a no. of new exptl. nucleoside analogs with activity against HBV. Unfortunately, fialuridine has been assocd. with severe mitochondrial damage and hepatotoxicity. Other stereoisomers may be more active and less toxic, but the potential danger of these drugs indicates that large scale clin. trials should proceed cautiously. Exptl. test systems for the preliminary investigation of antiviral compds. in hepatitis B and C will be required. ***Antisense*** ***oligodeoxyribonucleotides*** may inhibit the expression of the HBV genes. The natural history of ***hepatitis*** ***C*** is uncertain. Therapeutic trials of interferon-.alpha. indicated that a proportion of patients may respond to treatment with this agent. There is most information about 3 mU t.i.w. administered for 6 mo. It is not yet clear whether this dose is optimal. Multivariate anal. of several pretreatment parameters indicate that patients without cirrhosis are more responsive to interferon. The influence of genot.gamma..pi.es of ***hepatitis*** ***C*** is the subject of considerab.LAMBDA.e interest at present. Patients with diverse circulating quasispecies may be less responsive to therapy than those with a single major species. Improved responses have been obsd. in patients with lower levels of circulating ***hepatitis*** ***C*** virus RNA.

L22 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN AN 1995:190377 CAPLUS DN 122:231892

TI Detection and quantification of ***hepatitis*** ***C*** virus RNA replication in the liver
AU Sakamoto, Naoya; Enomoto, Nobuyuki; Kurosaki, Masayuki; Marumo, Fumiaki; Sato, Chifumi

CS Faculty of Medicine, Tokyo Medical and Dental University,
Tokyo, 113, Japan
SO Journal of Hepatology (1994), 20(5), 593-7 CODEN:
JOHEEC; ISSN: 0168-8278
DT Journal
LA English

AB To investigate the correlation between the replication of
hepatitis ***C*** virus in liver and the clin. and
histopathol. features, the authors detected and quantified plus
and minus strands of ***HCV*** -RNA in plasma and in livers
of patients with chronic ***hepatitis*** ***C*** by a
quant. polymerase chain reaction. RNA was extd. from the
plasma and liver tissue of ten patients with biopsy-proven chronic
hepatitis ***C***. The plus and minus strands of
HCV -RNA were detected by a strand-specific reverse
transcription with either sense or ***anti*** - ***sense***
oligonucleotide primers deduced from the
hepatitis ***C*** virus genome, and a std.
HCV -RNA with an enzyme restriction site was used to
quantify the amt. of ***HCV*** -RNA. Both plus and minus
strands of ***HCV*** -RNA were detected from the liver tissue
of all patients included. The amt. of plus-stranded ***HCV***
-RNA in the liver was 10 times higher than that of minus-
stranded ***HCV*** -RNA. Plus-stranded ***HCV*** -RNA
was detected in the plasma in all patients, while the minus strand
was not detected in any patient. There was a weak correlation
between the amt. of both strands of ***HCV*** -RNA in the
liver and that of the plus strand in plasma. There was no
significant correlation between the amt. of liver ***HCV*** -
RNA and serum alanine transaminase and aspartate transaminase
levels, or histopathol. findings in the liver. This method of
detecting and quantifying liver ***HCV*** -RNA is simple and
sensitive; it may be used to detect residual ***hepatitis***
C virus replication after the disappearance of plasma
HCV -RNA in acute hepatitis or in chronic hepatitis after
interferon treatment.

L22 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:317870 CAPLUS
DN 120:317870

TI Specific inhibition of ***hepatitis*** ***C*** virus
expression by ***antisense*** ***oligodeoxynucleotides***
. In vitro model for selection of target sequence
AU Wakita, Takaji; Wands, Jack R.
CS Mol. Hepatol. Lab., Harvard Med. Sch., Boston, MA, 02114,
USA

SO Journal of Biological Chemistry (1994), 269(19), 14205-10
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

AB The effect of sense and ***antisense***
oligodeoxynucleotides (ODNs) on ***hepatitis***
C virus (***HCV***) gene expression was studied to
det. the role of the highly conserved 5'-untranslated region in the
life cycle of the virus. It was found that ***antisense***
ODNs complementary to nucleotides (nt) 38-65, 134-175, and
312-339 in the 5' noncoding region and 341-377 in the core open
reading frame efficiently blocked ***HCV*** RNA translation.
Overlapping ODNs that differed by only several nucleotides
showed substantially different inhibition of ***HCV*** RNA
translation. Fine sequence specificity testing at nt positions 351-
377 revealed that ODNs as small as a 12-mer (nt 351-363)
retained a high degree (80%) of inhibitory activity compared to
ODNs of longer sequences. These results suggest that there are
three highly specific domains in the 5' noncoding region and a
sequence immediately downstream of the ***HCV*** core

initiation codon that may be crit. for translation of ***HCV***
RNA. This study also provides an exptl. approach for the
selection of target ***HCV*** RNA sequences susceptible to
antisense effects, as well as for definition of functional
regions of the genome necessary for viral replication.

L22 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1994:317330 CAPLUS

DN 120:317330

TI Amplification of RNA virus genome in a single container and
its detection

IN Yamaguchi, Kenjiro

PA Tonen Corp, Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp. CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	----	-----	-----

PI	JP 06046900	A2	19940222	JP 1992-222184	
	19920729				

PRAI	JP 1992-222184		19920729		
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AB A simplified method with reduced risk of contamination for
amplification and detection of RNA virus genome comprises (1)
extrn. of viral RNA in the presence of protein-degradating
enzymes, (2) prepn. of cDNA in the presence of reverse of
transcriptase, (3) amplification of the cDNA with PCR using 2 sets
of primers, (4) sizing and analyzing the PCR products by agarose
electrophoresis. A few sets of sense and ***antisense***
PCR primers are provided for detection of ***hepatitis***
C virus by this method. By this method, 30 samples/day
can be processed.

L22 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:642973 CAPLUS

DN 119:242973

TI ***Antisense*** ***oligonucleotides*** and
ribozymes for use in the inhibition of replication of viruses using
and RNA intermediate

IN Loss, Peter; Schreier, Peter; Maiss, Edgar; Schneider, Rudolf

PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften
e.V., Germany; Bayer A.-G.; Hoechst A.-G.

SO Eur. Pat. Appl., 19 pp. CODEN: EPXXDW

DT Patent

LA English

FAN.CNT	1	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE	-----	----	-----	-----

PI	EP 558944	A2	19930908	EP 1993-101710	
	19930204 EP 558944	A3	19940608	R: BE, CH, DE,	
	DK, FR, GB, IT, LI, NL DE 4203441	C1	19931014	DE	
	1992-4203441	19920206 AU 9332166	A1		
	19930812 AU 1993-32166	19930202 JP 06090758			
	A2 19940405 JP 1993-18498	19930205			
	PRAI DE 1992-4203441	A	19920206		

AB Oligoribonucleotides capable of binding to, and inhibiting
viral replication that passes through an RNA intermediate, are
described for use in improving the resistance of plants to
pathogenic viruses. These ***oligonucleotides*** may be
antisense ***oligonucleotides*** or ribozymes
capable of recognizing and cleaving these RNA intermediates and
they may be encoded on an heterologous virus that has been
rendered non-pathogenic or on integrating transforming DNA.
Synthetic DNA sequences encoding ribozymes capable of cleaving
the RNA of tomato spotted wilt virus were constructed by std.
phosphoramidite chem. and expression constructs introduced into

tobacco or potato protoplasts by Agrobacterium-mediated transformation. Transgenic tobacco plants challenged with the virus showed greatly reduced severity of infection and lower titers of viral antigens. The application of the method to animal cells is also demonstrated.

=> e kilkuskie r/au

E1	1	KILKUS STEPHEN P/AU
E2	1	KILKUSHIE ROBERT/AU
E3	0	--> KILKUSKIE R/AU
E4	2	KILKUSKIE R E/AU
E5	5	KILKUSKIE ROBERT/AU
E6	28	KILKUSKIE ROBERT E/AU
E7	1	KILKUSKIE ROBERT EDWARD/AU
E8	1	KILKUSKIE ROBERT L/AU
E9	1	KILKUYAMA SAKAE/AU
E10	1	KILL BETH/AU
E11	1	KILL BLOMHOFF HEIDI/AU
E12	1	KILL CLEMENS/AU

=> s e8

L23 1 "KILKUSKIE ROBERT L"/AU

=> e frank b/au

E1	1	FRANK AUSTEN K/AU
E2	1	FRANK AXEL/AU
E3	51	--> FRANK B/AU
E4	1	FRANK B A/AU
E5	22	FRANK B H/AU
E6	3	FRANK B S/AU
E7	34	FRANK BARBARA/AU
E8	1	FRANK BARRY M/AU
E9	2	FRANK BARRY W/AU
E10	1	FRANK BASIL/AU
E11	1	FRANK BASTIAN/AU
E12	2	FRANK BEATE/AU

=> e frank b l/au

E1	1	FRANK B A/AU
E2	22	FRANK B H/AU
E3	0	--> FRANK B L/AU
E4	3	FRANK B S/AU
E5	34	FRANK BARBARA/AU
E6	1	FRANK BARRY M/AU
E7	2	FRANK BARRY W/AU
E8	1	FRANK BASIL/AU
E9	1	FRANK BASTIAN/AU
E10	2	FRANK BEATE/AU
E11	3	FRANK BENJAMIN/AU
E12	5	FRANK BENJAMIN S/AU

=> e frank bruce/au

E1	9	FRANK BRIGITTA/AU
E2	1	FRANK BRIGITTE/AU
E3	9	--> FRANK BRUCE/AU
E4	83	FRANK BRUCE H/AU
E5	19	FRANK BRUCE HILL/AU
E6	13	FRANK BRUCE L/AU
E7	1	FRANK BRUCE LEONARD/AU
E8	1	FRANK BRUCE S/AU
E9	5	FRANK BRUNO/AU
E10	5	FRANK BRYAN/AU
E11	9	FRANK BRYAN C/AU
E12	1	FRANK BUEHLER/AU

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L24 23 "FRANK BRUCE"/AU OR "FRANK BRUCE L"/AU OR "FRANK BRUCE LEONARD"/AU

=> e goodchild j/au

E1	3	GOODCHILD I R/AU
E2	1	GOODCHILD IAN D/AU
E3	13	--> GOODCHILD J/AU
E4	1	GOODCHILD J A/AU
E5	1	GOODCHILD J C/AU
E6	3	GOODCHILD J H/AU
E7	1	GOODCHILD JANE/AU
E8	1	GOODCHILD JIM THOMPSON/AU
E9	61	GOODCHILD JOHN/AU
E10	1	GOODCHILD JOHN E/AU
E11	2	GOODCHILD JONATHAN A/AU
E12	2	GOODCHILD JOSIAH H/AU

=> s e3 or e10 or e9 13 "GOODCHILD J"/AU 1 "GOODCHILD JOHN E"/AU 61 "GOODCHILD JOHN"/AU
L25 75 "GOODCHILD J"/AU OR "GOODCHILD JOHN E"/AU OR "GOODCHILD JOHN"/AU

=> e wolfe j/au

E1	1	WOLFE ILONA/AU
E2	1	WOLFE INGRID/AU
E3	41	--> WOLFE J/AU
E4	5	WOLFE J A/AU
E5	1	WOLFE J ALAN/AU
E6	2	WOLFE J B/AU
E7	65	WOLFE J C/AU
E8	6	WOLFE J D/AU
E9	5	WOLFE J E/AU
E10	17	WOLFE J F/AU
E11	29	WOLFE J H/AU
E12	1	WOLFE J H N/AU

=> s e3

L26 41 "WOLFE J"/AU

=> e wolfe j l/au

E1	1	WOLFE J H N/AU
E2	6	WOLFE J K/AU
E3	2	--> WOLFE J L/AU
E4	32	WOLFE J M/AU
E5	3	WOLFE J N/AU
E6	1	WOLFE J O/AU
E7	161	WOLFE J P/AU
E8	1	WOLFE J PRESTON/AU
E9	3	WOLFE J R/AU
E10	10	WOLFE J R JR/AU
E11	1	WOLFE J S III/AU
E12	2	WOLFE J W/AU

=> s e3

L27 2 "WOLFE J L"/AU

=> e wolfe jia/au

E1	2	WOLFE JESSIE/AU
E2	1	WOLFE JESSIE MINAN/AU
E3	1	--> WOLFE JIA/AU
E4	4	WOLFE JIA L/AU
E5	14	WOLFE JIA LIU/AU
E6	1	WOLFE JOACHIM/AU
E7	1	WOLFE JOANNE/AU

E8 24 WOLFE JOE/AU
E9 1 WOLFE JOEL ZEV/AU
E10 10 WOLFE JOHN/AU
E11 7 WOLFE JOHN A/AU
E12 16 WOLFE JOHN C/AU

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L28 19 "WOLFE JIA"/AU OR "WOLFE JIA L"/AU OR "WOLFE JIA LIU"/AU

=> e roberts p c/au

E1 6 ROBERTS P ANN/AU
E2 30 ROBERTS P B/AU
E3 6 --> ROBERTS P C/AU
E4 1 ROBERTS P C B/AU
E5 6 ROBERTS P C T/AU
E6 1 ROBERTS P CHRISTOPHER/AU
E7 41 ROBERTS P D/AU
E8 18 ROBERTS P E/AU
E9 11 ROBERTS P ELAINE/AU
E10 6 ROBERTS P F/AU
E11 6 ROBERTS P G/AU
E12 33 ROBERTS P H/AU

=> s e3

L29 6 "ROBERTS P C"/AU

=> e roberts peter/au

E1 1 ROBERTS PEREDUR J P/AU
E2 2 ROBERTS PERRY L/AU
E3 39 --> ROBERTS PETER/AU
E4 7 ROBERTS PETER A/AU
E5 24 ROBERTS PETER B/AU
E6 9 ROBERTS PETER C/AU
E7 1 ROBERTS PETER C T/AU
E8 1 ROBERTS PETER CLAYTON/AU
E9 2 ROBERTS PETER CLIVE B/AU
E10 1 ROBERTS PETER CLIVE BUCKLEY/AU
E11 2 ROBERTS PETER D/AU
E12 3 ROBERTS PETER F/AU

=> s e3 or e6 or e8 39 "ROBERTS PETER"/AU 9
"ROBERTS PETER C"/AU 1 "ROBERTS PETER CLAYTON"/AU
L30 49 "ROBERTS PETER"/AU OR "ROBERTS PETER C"/AU
OR "ROBERTS PETER CLAYTON"/AU

=> e hamlin h a/au

E1 1 HAMLIN GREEN G/AU
E2 2 HAMLIN GREEN GINA/AU
E3 1 --> HAMLIN H A/AU
E4 1 HAMLIN H ALLEN JR/AU
E5 1 HAMLIN H C/AU
E6 2 HAMLIN H F/AU
E7 5 HAMLIN H P/AU
E8 1 HAMLIN H S/AU
E9 1 HAMLIN H SCOTT/AU
E10 2 HAMLIN HENRY A/AU
E11 1 HAMLIN HENRY A JR/AU
E12 1 HAMLIN HERBERT SCOTT/AU

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"HAMLIN H ALLEN JR"/AU 2 "HAMLIN HENRY A"/AU 1
"HAMLIN HENRY A JR"/AU
L31 5 "HAMLIN H A"/AU OR "HAMLIN H ALLEN JR"/AU OR
"HAMLIN HENRY A"/AU OR "HAMLIN HENRY A JR"/AU

=> e roberts n a/au

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E2 36 ROBERTS N/AU
E3 37 --> ROBERTS N A/AU
E4 53 ROBERTS N B/AU
E5 5 ROBERTS N E/AU
E6 1 ROBERTS N ELIZABETH/AU
E7 3 ROBERTS N F/AU
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E9 2 ROBERTS N J JR/AU
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E12 2 ROBERTS N M/AU

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L32 73 "ROBERTS N"/AU OR "ROBERTS N A"/AU

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E1 13 ROBERTS NIRA R/AU
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E3 7 --> ROBERTS NOEL/AU
E4 26 ROBERTS NOEL A/AU
E5 4 ROBERTS NOEL ALLAN/AU
E6 11 ROBERTS NOEL K/AU
E7 1 ROBERTS NOELLE/AU
E8 34 ROBERTS NORBERT J JR/AU
E9 2 ROBERTS NORM/AU
E10 1 ROBERTS NORMAL B/AU
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E12 25 ROBERTS NORMAN B/AU

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OR "ROBERTS NOEL ALLAN" /AU

=> e walther d m/au

E1 12 WALTHER D C/AU
E2 1 WALTHER D J/AU
E3 10 --> WALTHER D M/AU
E4 2 WALTHER DAGMAR/AU
E5 1 WALTHER DAGNY/AU
E6 1 WALTHER DANE/AU
E7 2 WALTHER DANE S/AU
E8 1 WALTHER DANE STUART/AU
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E10 5 WALTHER DAVID C/AU
E11 4 WALTHER DEBRA M/AU
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L34 14 "WALTHER D M"/AU OR "WALTHER DEBRA M"/AU

=> d his

(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
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L2 13330 S (HEPATITIS(W)C)/BI,AB
L3 13947 S L1 OR L2
L4 10 S ODN3/BI,AB
L5 75023 S OLIGONUCLEOTIDE#/BI,AB
L6 7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7 9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB

L8 82587 S L4 OR L5 OR L6 OR L7
L9 596 S L3 AND L8
L10 38114 S ANTISENSE/BI,AB
L11 1297 S (ANTI(W)SENSE)/BI,AB
L12 38918 S L10 OR L11
L13 19463 S L8 AND L12
L14 166 S L9 AND L12
L15 136 S L14 NOT 2005/PY
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E FRANK BRUCE/AU
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L30 49 S E3 OR E6 OR E8 E HAMLIN H A/AU
L31 5 S E3 OR E4 OR E10 OR E11 E ROBERTS N
A/AU
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L33 37 S E3 OR E4 OR E5 E WALTHER D M/AU
L34 14 S E3 OR E11

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l32 or l33 or l34

L35 317 L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29
OR L30 OR L31 OR L32 OR L33 OR L34

=> s l3 and l35

L36 5 L3 AND L35

=> d l36 1-5 bib ab

L36 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:488123 CAPLUS

DN 137:73234

TI Oligonucleotides specific for ***hepatitis*** ***C***
virus treatment

IN ***Kilkuskie, Robert L.*** ; ***Frank, Bruce L.*** ;
Goodchild,

*** John*** ; ***Wolfe, Jia L.*** ; ***Roberts, Peter
C.*** ; ***Hamlin, Henry A.*** ; ***Roberts, Noel A.*** ;
Walther, Debra

*** M.***

PA USA

SO U.S. Pat. Appl. Publ., 74 pp., Cont.-in-part of U.S. Ser. No.
471,968. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI	US 2002081577	A1	20020627	US 1997-887505
	19970702 EP 1331267	A2	20030730	EP 2003-5364
	19960604 EP 1331267	A3	20031203	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI	US 1995-471968	A2	19950606	US 1996-21104P
P	19960702 EP 1996-920788	A3	19960604	

AB The invention discloses synthetic oligonucleotides
complementary to contiguous and non-contiguous regions of the
HCV RNA. Also disclosed are methods and kits for
inhibiting the replication of ***HCV***, inhibiting the
expression of ***HCV*** nucleic acid and protein, and for
treating ***HCV*** infections.

L36 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:471834 CAPLUS

DN 133:86096

TI Enhancement of ribozyme catalytic activity with 2'-O-
substituted facilitator oligonucleotide

IN ***Goodchild, John***

PA University of Massachusetts Worcester, USA

SO U.S., 15 pp., 5612469 Cont.-in-part of U.S. 5,612,469.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE			

PI	US 6087484	A	20000711	US 1997-819942
	19970318 US 5612469	A	19970318	US 1995-431625
	19950501			

PRAI	US 1992-830713	B1	19920204	US 1993-138896
B1	19931019	US 1995-431625	A2	19950501

AB Methods are disclosed for increasing ribozyme catalytic
activity without reducing specificity, which methods comprise
contacting an RNA mol. with a ribozyme and a 2'-O-substituted
facilitator oligonucleotide. The facilitator oligonucleotide binds to
the substrate RNA at a site contiguous to the ribozyme binding
site. The present invention further provides compns. comprising
a ribozyme and an effective amt. of a 2'-O-Me substituted
facilitator oligonucleotide. The use of a facilitator, particularly a
2'-O-substituted facilitator, and more esp. a 2'-O-Me substituted
facilitator, greatly enhances ribozyme catalytic activity, frequently
making an otherwise inactive ribozyme active. The method was
demonstrated with ribozymes targeted to HIV-1 and
hepatitis ***C*** virus RNAs as well as to VEGF
mRNA. Both length and presence/absence of 2'-O-Me groups in
the oligoribonucleotide facilitator affected the efficiency of
substrate cleavage.

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE
FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L36 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:290674 CAPLUS

DN 127:23730

TI Efficient removal of viruses by a novel polyvinylidene fluoride
membrane filter

AU ***Roberts, Peter***

CS Res. & Development Dep., Bio Products Lab., Herts, WD6
3BX, UK

SO Journal of Virological Methods (1997), 65(1), 27-31 CODEN:
JVMEHJ; ISSN: 0166-0934

PB Elsevier

DT Journal

LA English

AB Virus removal by a novel filter (Ultipor VF DV50), comprising
3 layers of PVDF membrane, was evaluated by infectivity studies
using a range of viruses and conditions. The filter was able to
remove at least 6 log of various viruses, i.e., Sindbis and Semliki
Forest (40-70 nm), herpes simplex (120-200 nm), and vaccinia
(200 x 350 nm), from cell-culture medium or phosphate-buffered
saline, pH 6.8, contg. 0.5% albumin. However, the removal of

polio virus (25-30 nm) under these conditions was only limited, i.e., about 1 log. This filter is thus effective for removing viruses of about 50 nm or larger. Proteins as large as Igs (MW 160, 000), were able to pass through the filter with recoveries of at least 85%. Due to its ability to remove viruses of medium-to-large size, this filter shows potential for increasing the safety of biol. products where viruses such as hepatitis B, C, herpes, and retroviruses are of concern.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L36 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN AN 1997:124382 CAPLUS DN 126:126887

TI ***Hepatitis*** ***C*** virus-complementary oligonucleotides and analogs and their use in prophylaxis, treatment and diagnosis of viral infection
IN ***Frank, Bruce L.*** ; ***Goodchild, John*** ; ***Hamlin, Henry***
*** A., Jr.*** ; Kilkuskie, Robert E. ; ***Roberts, Noel A.*** ; ***Roberts, Peter C.*** ; ***Walther, Debra M.*** ; ***Wolfe, Jia***
*** L.***

PA F. Hoffmann-La Roche Ag, Switz.; Hybridon Inc.
SO PCT Int. Appl., 99 pp. CODEN: PIXXD2
DT Patent
LA English

FAN.CNT	2	PATENT NO.	KIND	DATE	APPLICATION
NO.	DATE				

PI	WO 9639500	A2	19961212	WO 1996-EP2427
	19960604 WO 9639500	A3	19970313	W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, VZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG ZA 9604446 A 19961206 ZA 1996-4446 19960530 CA 2226438 AA 19961212 CA 1996-2226438 19960604 AU 9662219 A1 19961224 AU 1996-62219 19960604 EP 833902 A2 19980408 EP 1996-920788 19960604 EP 833902 B1 20030514 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI AT 240392 E 20030515 AT 1996-920788 19960604 EP 1331267 A2 20030730 EP 2003-5364 19960604 EP 1331267 A3 20031203 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI PT 833902 T 20030930 PT 1996-920788 19960604 ES 2196157 T3 20031216 ES 1996-920788 19960604 PRAI US 1995-471968 A 19950606 EP 1996-920788 A3 19960604 WO 1996-EP2427 W 19960604

AB The present invention discloses synthetic oligonucleotides and oligonucleotide analogs complementary to contiguous and non-contiguous regions of the ***hepatitis*** ***C*** virus (***HCV***) RNA. Also disclosed are methods and kits for inhibiting the replication of ***HCV***, inhibiting the expression of ***HCV*** nucleic acid and protein, and for treating ***HCV*** infections. Numerous oligodeoxyribonucleotides, hybrid oligodeoxy- and deoxyribonucleotides, and analogs of these oligonucleotides contg. modified linkages, modified bases, modified sugar residues, etc. were prep'd. These oligonucleotides were tested in RNase H cleavage assays as well as in inhibition of ***HCV*** luciferase fusion protein expression in stably transfected cells,

inhibition of ***HCV*** RNA expression in stably transfected cells, and inhibition of ***HCV*** protein expression in Semliki Forest virus/ ***HCV*** recombinant virus infected cells. Sequence-specific inhibition was obsd.

L36 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN AN 1995:569922 CAPLUS DN 123:28287
TI An in vitro assay for ***hepatitis*** ***C*** virus NS3 serine proteinase
AU Bouffard, Pascal; Bartenschlager, Ralf; Ahlborn-Laake, Ludwina; Mous, Jan; ***Roberts, Noel*** ; Jacobsen, Helmut CS Antiviral Biol. Dept., Roche Products, Ltd., Herts, AL7 3AY, UK
SO Virology (1995), 209(1), 52-9 CODEN: VIRLAX; ISSN: 0042-6822
PB Academic
DT Journal
LA English
AB ***Hepatitis*** ***C*** virus (***HCV***) encodes a polypeptide of which the majority of nonstructural proteins are matured by the viral serine proteinase located in the N terminus of NS3. Intracellular studies using recombinant vaccinia virus have shown that both NS3 and its cofactor NS4A are required to enhance processing at the NS3-dependent cleavage sites. We developed an in vitro (cell-free) assay in which the ***HCV*** serine proteinase was shown to be enzymically active, by mixing lysates of cells expressing either the serine proteinase or a nonstructural protein substrate. NS3 cleaved in a highly reproducible manner at the NS5A/5B site in the presence of NS4A, whereas NS3 alone was enzymically inactive. NS4A could be provided either linked to NS3 or as part of the substrate. In contrast, irresp. of the presence or absence of NS4A, no NS3-mediated processing was obsd. at the NS3/4A, NS4A/4B, and NS4B/5A sites in this assay. In vitro cleavage at the NS5A/5B site occurred rapidly, within 1 min at temps. ranging from 0 to 20.degree., but was incomplete and required detergent-solubilized lysates. General serine proteinase inhibitors did not decrease processing activity. The in vitro model described in this study is a new tool: (1) to study the structure and the function of ***HCV*** serine proteinase and NS5A/5B cleavage site, and (2) to test NS3 serine proteinase inhibitors.

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(FILE 'HOME' ENTERED AT 16:40:38 ON 27 APR 2005)
FILE 'CAPLUS' ENTERED AT 16:40:48 ON 27 APR 2005

L1	9043 S HCV/BI,AB
L2	13330 S (HEPATITIS(W)C)/BI,AB
L3	13947 S L1 OR L2
L4	10 S ODN3/BI,AB
L5	75023 S OLIGONUCLEOTIDE#/BI,AB
L6	7363 S OLIGODEOXYNUCLEOTIDE#/BI,AB
L7	9483 S OLIGODEOXYRIBONUCLEOTIDE#/BI,AB
L8	82587 S L4 OR L5 OR L6 OR L7
L9	596 S L3 AND L8
L10	38114 S ANTISENSE/BI,AB
L11	1297 S (ANTI(W)SENSE)/BI,AB
L12	38918 S L10 OR L11
L13	19463 S L8 AND L12
L14	166 S L9 AND L12
L15	136 S L14 NOT 2005/PY
L16	99 S L15 NOT 2004/PY
L17	82 S L16 NOT 2003/PY
L18	66 S L17 NOT 2002/PY
L19	49 S L18 NOT 2001/PY

L20 38 S L19 NOT 2000/PY
L21 27 S L20 NOT 1999/PY
L22 18 S L21 NOT 1998/PY E KILKUSKIE R/AU
L23 1 S E8 E FRANK B/AU E FRANK B L/AU
E FRANK BRUCE/AU
L24 23 S E3 OR E6 OR E7 E GOODCHILD J/AU
L25 75 S E3 OR E10 OR E9 E WOLFE J/AU
L26 41 S E3 E WOLFE J L/AU
L27 2 S E3 E WOLFE JIA/AU
L28 19 S E3 OR E4 OR E5 E ROBERTS P C/AU
L29 6 S E3 E ROBERTS PETER/AU
L30 49 S E3 OR E6 OR E8 E HAMLIN H A/AU
L31 5 S E3 OR E4 OR E10 OR E11 E ROBERTS N
A/AU
L32 73 S E2 OR E3 E ROBERTS NOEL/AU
L33 37 S E3 OR E4 OR E5 E WALTHER D M/AU
L34 14 S E3 OR E11
L35 317 S L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR
L29 OR L30 OR L31 O
L36 5 S L3 AND L35

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COST IN U.S. DOLLARS	SINCE FILE
TOTAL	ENTRY SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE
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SESSION	
CA SUBSCRIBER PRICE	-16.79 -16.79

STN INTERNATIONAL LOGOFF AT 16:51:51 ON 27 APR 2005